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10/584,393	11/21/2006	Naoko Horikoshi	1004451.001US (4439-4045)	3674

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EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
07/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/584,393	HORIKOSHI ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. BABIC	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 11-18* is/are pending in the application.

4a) Of the above claim(s) *5-8,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 9, 11-15, and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claim(s) 1, 2, 4-9, and 11-18 are pending. Claim(s) 1, 2, 4, 9, 11-15, and 18 are under examination. Upon review of the prosecution history it was discovered that claim 16 should be withdrawn because it contains SEQ ID NOs that were not elected from the restriction requirement issued March 26, 2009. Thus, claims 5-8, 16, and 17 are withdrawn from consideration. The following Office Action is in response to Applicant's communication dated April 27, 2010. The following Office Action is NON-FINAL due to the new grounds of rejection presented below.

Examiner of Record

As an initial matter, it is noted that the examiner of record has been changed from Khatol S. Shahnan-Shah, Art Unit 1645, to Christopher M. Babic, Art Unit 1637.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 18, 2010 was filed after the mailing date of the NON-FINAL Office Action on January 27, 2010. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Applicant is advised that if an English translation of a cited foreign language reference is not provided, it will not be considered. Abstracts will be considered if a proper translation is provided.

Claim Rejections - 35 USC § 112 - Indefiniteness - New Grounds

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 1, 2, 4, 9, 11-15, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The metes and bounds of claim 1 are indefinite because it is unclear what constitutes a buffer with "similar" ability. In other words, a person of ordinary skill in the art would not be reasonably apprised of the range of "similar" buffers.

(b) With regard to claim 13, an Applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) . In the instant case, the examiner can find no clear definition of term “Enterolysine" in the specification or related art (i.e. prior

and post filing date). Thus, the term is indefinite because the specification does not clearly define the new term.

Claim Rejections - 35 USC § 103 - Withdrawn

Applicant's claim amendments and supplemental remarks are sufficient to overcome the rejection of claim(s) 1-4, 9-16, and 18 over Anzar and Brahser.

Claim Rejections - 35 USC § 103 - New Grounds

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim(s) 1, 2, 9, 11, 12, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsih et al. (J Food Prot. 2001 Nov;64(11):1744-50) in view of Kearney et al. (U.S. 5,589,335), and in further view of Brasher et al. (Curr Microbiol. 1998 Aug;37(2):101-7).

Hsih teaches methods of detecting *Salmonella typhimurium* and *Listeria monocytogenes* comprising: (a) extracting DNA; and (b) performing multiplex PCR (pg. 1745, col. 2, multiplex PCR conditions, for example). The reference expressly teaches that UP broth was used such that both bacteria could grow simultaneously (pg. 1745, col. 1, culture conditions). The UP broth appears analogous to the medium No. 17 used by Applicant on pg. 23 of specification (0.5 g glucose).

Hish does not expressly teach treating bacterial samples with a lytic enzyme, a surfactant, and a protein denaturant.

Kearney provides a supportive disclosure that teaches lysing a bacterial sample comprising *E. coli* and *L. monocytogenes* with lysozyme, bacteriocin, and proteinase K (col. 17, lines 50-65, for example).

None of the above references expressly teach the use of a surfactant during cellular lysis.

Brasher provides a supportive disclosure that teaches lysing a bacterial sample comprising *E. coli* and *S. typhimurium* with SDS and proteinase K followed by centrifugation and DNA precipitation with alcohol (pg. 102, col. 1, genomic DNA extraction, for example).

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to utilize a combination of a lysozyme, bacteriocin, surfactant, and protein denaturant to lyse the bacterial samples of Hsih since the prior art exemplifies each reagent as useful for lysing the different types of bacteria in Hsih.

Applicant is reminded that the "teaching, suggestion, or motivation" (TSM) test should not be applied as a rigid formula for determination of obviousness. In a recent case before the Supreme Court, *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the court addressed the TSM test, reciting the following,

"The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility."

Furthermore, in *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 80 USPQ2d 1641 (Fed. Cir. 2006), the court found that,

"Our suggestion test is in actuality quite flexible and not only permits, but requires, consideration of common knowledge and common sense,...,Indeed, we have repeatedly held that an implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the “improvement” is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal—and even common-sensical—we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan

possesses knowledge and skills rendering him capable of combining the prior art references,...,Persons of varying degrees of skill not only possess varying bases of knowledge, they also possess varying levels of imagination and ingenuity in the relevant field, particularly with respect to problem-solving abilities."

Thus, the courts have concluded that any reasoned argument grounded in the analysis set forth in *Graham et al. v. John Deere Company of Kansas City et al.*, 148 USPQ 459 (U.S. 1966), may form the basis for a *prima facie* case of obviousness.

In the instant case, a person of ordinary skill in the art would have possessed the knowledge necessary to create the claimed lysis combination to lyse the different bacteria of Hsih in a reasonably predictable manner.

2. Claim(s) 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hsih et al. (J Food Prot. 2001 Nov;64(11):1744-50) in view of Kearney et al. (U.S. 5,589,335), in view of Brasher et al. (Curr Microbiol. 1998 Aug;37(2):101-7) as applied to claim 1 above, and in further view of Rimick et al. (U.S. 6,468,743 B1) , in view of Buck et al ("Design Strategies and Performance of Custom DNA Sequencing Primers" Biotechniques. 1999. 27(3): pages 528-536), and in further view of Lowe et al. (Nucleic Acids Research, Vol. 18, No. 7, page 1757-1761, 1990).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach the primer sequences recited in SEQ ID NOs: 5 and 6.

However, it is first noted that the *L. monocytogenes* target sequence for example, the sequence from which the claimed oligonucleotides were derived, is a sequence that

was well known at the time of invention (see Rimick SEQ ID NO: 59). Thus, the binding site of SEQ ID NOs: 5 for example is suggested within the sequence disclosed by Rimick (see alignment of Rimick SEQ ID NO: 59 with SEQ ID NO: 5 for example below).

```
RESULT 2
AR238655
LOCUS       AR238655                  40 bp    DNA     linear   PAT 20-DEC-2002
DEFINITION  Sequence 59 from patent US 6468743.
ACCESSION   AR238655
VERSION     AR238655.1  GI:27283725
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 40)
  AUTHORS   Romick,T.L. and Fraser,M.S.
  TITLE     PCR techniques for detecting microbial contaminants in foodstuffs
  JOURNAL   Patent: US 6468743-A 59 22-OCT-2002;
            ConAgra Grocery Products Company; Fullerton, CA
FEATURES             Location/Qualifiers
     source          1. .40
                     /organism="unknown"
                     /mol_type="genomic DNA"
ORIGIN

  Query Match             100.0%;  Score 20;  DB 2;  Length 40;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CGGAGGTTCCGCAAAAGATG 20
              ||||||||||||||||||||
Db          1 CGGAGGTTCCGCAAAAGATG 20
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Applicant is directed to *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed sequences simply represent structural homologs of those sequences disclosed in the prior art, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers (SEQ ID NOs: 5 and 6) is *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck provides a supporting disclosure that expressly presents evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

In addition to teachings of Buck, Lowe provides a supportive disclosure that teaches a method for designing primers and evaluating their performance wherein a computer program is used for rapid selection of oligonucleotide primers for polymerase chain reaction (see page 1757, col. 1, abstract). The reference teaches that all primers designed for over 10 gene products were experimentally tested and the results showed that all the amplification products specified by the primers are of the predicted size and also hybridize with the appropriate cDNA or internal oligonucleotide probe (see page 1760, col. 2, paragraph 1).

As explained above, the claimed sequences simply represent structural homologs of those sequences disclosed in the prior art, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers (SEQ ID NOs: 5 and 6) are *prima facie* obvious over the cited references in the absence of secondary considerations.

Furthermore, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention, to combine the known *L. monocytogenes* nucleic acid sequences as taught by the prior art with a step of generating and designing primers as taught by Hsih to detect the presence of *L. monocytogenes* because such genomic sequences were known (Rimick) at the time the invention was made, and it is obvious to generate primers from known sequences as taught by Lowe. The ordinary artisan would have had a reasonable expectation of success that such primers or primer pairs generated using known sequences as taught by Rimick in view of Lowe to amplify *L. monocytogenes* sequences for detection because the claimed primers are functional

equivalents of the sequences taught by Hsih, Rimick, and Lowe explicitly taught that all primers designed for over 10 gene products were experimentally tested and the results showed that all the amplification products specified by the primers are of the predicted size (see page 1760, col. 2, paragraph 1). The ordinary artisan would have been motivated to generate a number of said primers and primer pairs for detection of *L. monocytogenes* sequences to provide flexibility and optimize experimentation. Selection of specific oligonucleotides for specific T_m represents routine optimization with regard to sequence, length and composition of the oligonucleotide. Such optimization parameters are explicitly recognized in Lowe (This clearly shows that every primer would have a reasonable expectation of success). As noted in *In re Aller*, 105 USPQ 233 at 235, more particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the primer selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

It is noted that a sufficient showing of a secondary consideration (e.g. unexpected results) would obviate this and any further rejection of this type. Submission of a secondary consideration such as latent properties must be supported by objective evidence of a probative value (see MPEP 716.01).

3. Claim(s) 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hsih et al. (J Food Prot. 2001 Nov;64(11):1744-50) in view of Kearney et al. (U.S. 5,589,335), in view of Brasher et al. (Curr Microbiol. 1998 Aug;37(2):101-7) as applied to claim 1 above, and in further view of Bussey et al. (U.S. 6,011,148).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach the use of Tween 20.

Bussey provides a supportive disclosure that teaches,

"...plasmid DNA may be isolated from bacterial sources using conventional procedures including lysis with alkali and/or detergents, e.g. SDS, NP40, Tween 20 and the like, mechanical methods, or boiling, followed by precipitation of proteins, chromosomal DNA and cell debris. (see Sambrook, et al., 1989; Carlson et al., 1995, Biotech. Bioeng. 48: 303-315; Hirt, 1967, J. Mol. Biol. 26: 365-369)." (col. 5)

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to utilize Tween 20 in the lysis mixture of Hsih since the prior art highlights Tween 20 as a functional equivalent of SDS.

4. Claim(s) 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hsih et al. (J Food Prot. 2001 Nov;64(11):1744-50) in view of Kearney et al. (U.S. 5,589,335), in view of Brasher et al. (Curr Microbiol. 1998 Aug;37(2):101-7) as applied to claim 1 above, and in further view of Anzar et al. (Syst Appl Microbiol. 2002 Apr;25(1):109-19).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach the use of guanidium isothiocyanate.

Anzar provides a supportive disclosure that teaches lysing a bacterial sample comprising *L. monocytogenes* with guanidium isothiocyanate (pg. 110, col. 2, DNA isolation, for example).

Thus, in summary, it is submitted that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to utilize guanidium isothiocyanate in the lysis mixture of Hsih since the prior art highlights guanidium isothiocyanate as a functional equivalent of proteinase K.

Prior Art

Claim 13 is free of the prior art but rejected for other reasons. Claim 13 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 814-880-9945. The examiner can normally be reached on Monday-Friday 10:00AM to 6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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